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07/402,450	09/01/89	MURAKAWA G	

EXAMINER	
ESCALLON, M	
ART UNIT	**PAPER NUMBER**
187	9

DATE MAILED: 09/04/91

EDWARD S. IRONS
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WASHINGTON, DC 20006

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☑ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ____ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☑ Claims 1 - 30 are pending in the application.
   Of the above, claims 1 - 17 are withdrawn from consideration.
2. ☑ Claims 1 - 17 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 18 - 30 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Receipt of the amendment to cancel claims 1-17 filed June 6, 1991 is acknowledged. The amendment to "disregard the amendment before action" has not been considered or entered. Applicants are directed to MPEP 608.01(s) that reads:

> "Canceled text in the specification or canceled claims can be restored only by presenting the canceled matter as a new insertion. See 37 CFR 1.124, MPEP § 714.24."

Applicants are requested to look over the specification and correct any minor errors without adding new matter.

Applicants are encouraged to file an information disclosure statement including (1) a form PTO-1449, "Information Disclosure Citation" listing patents, publications, seminars, and other information material to the instant application; (2) a concise explanation of the relevance of each listed item; and (3) a copy of each listed item as a means of complying with the duty of disclosure set forth in 37 CFR 1.56. See 37 CFR 1.97 through 1.99 and MPEP 609.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure.

There is no enablement of the phrase "process for minimizing false negative data". There is no support in the specification for applicants phrase which is absent any explanation or demonstration of how said "minimizing" false positives is accomplished.

Claims 18-30 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the sequences disclosed on pages 4-6 of the specification. See M.P.E.P. §§ 706.03(n) and 706.03(z). Applicants have provide a series of isolated primers corresponding to specific conservative regions of HIV and HMCV viruses. It would require undue experimentation to one of ordinary skill in the art to select other sequences and select primers which function the same in the present application.

Claims 18-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is vague and confusing. The construction of "synthetic RNA" is unstated. The length of the "target" is unstated, i.e., two nucleotides? It is unclear whether "substantially more" will include the target contradicting the prior statement. The phrase "said reference sequence" lack of antecede basis. It is unclear which is the "reference sequence" that applicants intended to use i.e. the target or the synthetic

sequence.

Claims 18 and 19 are indefinite. T-cell receptor or beta acting genes are sequences known in the art and which are characterized by considerable length. Applicants fail to particularly point out and distinctly claim what they regard as their invention. Part (ii) in claim 19 is confusing and indefinite. It is unclear if applicants intention is to amplify any RNA present in the sample even if the cell have not been infected by virus. Part (iii) in claim 19 is indefinite. It is not clear to what applicants are referring by a "construct multi-base insertion" and the specification gives no guidance as how this construct has been made.

Claims 20-25 are vague. Applicants' claims recite "a target sequence located in a region". The relative positions of the target sequences is not given but is important for proper operation of the invention. That is, a 35 U.S.C. 101 operatibility criticism can arise unless the specific sequence or the relative position of the sequence within the region is known as those disclosed in the specification on pages 4-6.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 is rejected under 35 U.S.C. § 102(b) as being

clearly anticipated by Mullis et al.

Mullis et al. disclose the amplification of viral RNA in the bridging sentences between columns 7 and 8. Mullis et al. cite the use of both reverse transcriptase and Klenow fragment as agents of polymerization in column 10, lines 7-17. Additionally, column 10, lines 7-9, clearly directs the practitioner to practice either a "system" or "enzymes" to effect extension product synthesis due to the exclusive use of deoxyribonucleotide triphosphates as given in column 9, lines 50-54, as is also the only instantly enabled synthesis method. In the above method is disclosed the alternative adding of either one or two primers so as to facilitate the second strand synthesis from a single stranded target sequence, followed by amplification of both strands by two primers, in column 9, lines 5-49. The whole process is summarized by Mullis et al. in column 2, line 63, through column 3, line 33, wherein the detection step with a labeled probe is cited in column 3, lines 25-27.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 18-23 and 26-30 are rejected under 35 U.S.C. § 103 as being unpatentable over Mullis et al. in view of Rathner et al.

The instant invention is directed to PCR detection of HIV target sequences including some regions being claimed as to primers and probe.

Mullis et al. is a general but very detailed teaching as to the PCR method and is summarized above. Rathner et al. give the complete HIV genomic sequence as well as discussion of regions contained therein.

Mullis et al. disclose the practice of PCR which includes the amplification method instantly claimed but does not specifically cite HIV target amplification or the instantly 3'ORF, beta actin, T-7 RNA polymerase, primers and probes. Mullis et al. discuss the amplification of a target which is a portion of a larger molecule in a column 7, lines 47-49. However, in column 8, line 9-19, it is taught that primer preparation requires only the knowledge of the appropriate target sequences. Rathner et al. disclose the entire HIV genomic sequence which clearly therefore gives the required knowledge for not only many possible primer sequences but probes as well. Thus, it would have been obvious to one of ordinary skill in the art at the time of

the instant invention to apply the PCR technique of Mullis et al. to HIV amplification and detection because Mullis et al. supply the general technique with a great deal of guidance as to its application and Rathner et al. supplies the sequence information which is the last required data for the use of PCR in HIV amplification and detection.

Claim 24 and 25 are rejected under 35 U.S.C. § 103 as being unpatentable over Mullis et al in view of Rathner et al. as applied to claim 18-23 and 26-30 above, and further in view of Hennighausen et al. and Waten et al.

Mullis et al. and Rathner et al. have been fully outlined above.

Hennighausen et al. give the complete HCMV immediate early (IE1) genomic sequence as well as discussion of regions contained therein. Wathen et al. give probes that hybridize late HCMV genes as well as a discussion of regions contained therein. As applied above, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to apply the PCR technique of Mullis et al. to HMCV amplification and detection because Mullis et al. supply the general technique with a great deal of guidance as to its application and Hennighausen et al. and Waten et al. supply the sequence information which is the last required data for the use of PCR in HCMV (IE) or late regions for amplification and detection.

Claims 18-30 are provisionally rejected under the judicially

created doctrine of obviousness-type double patenting as being unpatentable over claims 24-53 of copending application Serial No. 07/180,740. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are directed to detect an RNA virus via PCR methodology with primers and probes of conserved transcript sequences that are known in the prior art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The obviousness-type double patenting rejection is a judicially established doctrine based upon public policy and is primarily intended to prevent prolongation of the patent term by prohibiting claims in a second patent not patentably distinct from claims in a first patent. In re Vogel, 164 USPQ 619 (CCPA 1970). A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) would overcome an actual or provisional rejection on this ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. § 1.78(d).

Claims 18-30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-16 of copending application Serial No. 07/355,296. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the same reasons set forth above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier

communications from the examiner should be directed to Miguel H. Escallon, Ph.D. whose telephone number is (703) 308-3890.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

M.H.E.
August 26, 1991

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
ART UNIT 187